

pRL4

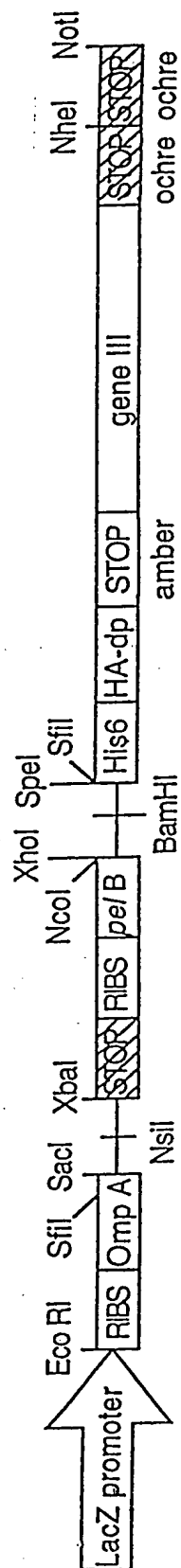


Fig. 1

Human Antibody sequence (TT sequence) (SEQ ID NO: 54)

Heavy Chain: cloning sites Xho I and Spe I are underlined

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1
gag gtg cag ctg CTC GAG CAG TCT GGG GCT GAG GTG AAG AAG CCT GGG TCC TCG GTG AAG
glu val gln leu leu glu gln ser gly ala glu val lys lys pro gly ser ser val lys
21
GTC TCC TGC AGG GCT TCT GGA GGC ACC TTC AAC AAT TAT GCC ATC AGC TGG GTG CGA CAG
val ser cys arg ala ser gly gly thr phe asn asn tyr ala ile ser trp val arg gln
41
GCC CCT GGA CAA GGG CTT GAG TGG ATG GGA GGG ATC TTC CCT TTC CGT AAT ACA GCA AAG
ala pro gly gln gly leu glu trp met gly gly ile phe pro phe arg asn thr ala lys
61
TAC GCA CAA CAC TTC CAG GGC AGA GTC ACC ATT ACC GCG GAC GAA TCC ACG GGC ACA GCC
tyr ala gln his phe gln gly arg val thr ile thr ala asp glu ser thr gly thr ala
81
TAC ATG GAG CTG AGC AGC CTG AGA TCT GAG GAC ACG GCC ATA TAT TAT TGT GCG AGA GGG
tyr met glu leu ser ser leu arg ser glu asp thr ala ile tyr tyr cys ala arg gly
101
GAT ACG ATT TTT GGA GTG ACC ATG GGA TAC TAC GCT ATG GAC GTC TGG GGC CAA GGG ACC
asp thr ile phe gly val thr met gly tyr tyr ala met asp val trp gly gln gly thr
121
ACG GTC ACC GTC TCC GCA GCC TCC ACC AAG GGC CCA TCG GTC TTC CCC cTG GCA CCC TCC
thr val thr val ser ala ala ser thr lys gly pro ser val phe pro leu ala pro ser
141
TCC AAG AGC ACC TCT GGG GGC ACA GCG GCC CTG GGC TGC CTG GTC AAG GAC TAC TTC CCC
ser lys ser thr ser gly gly thr ala ala leu gly cys leu val lys asp tyr phe pro
161
GAA CCG GTG ACG GTG TCG TGG AAC TCA GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG
glu pro val thr val ser trp asn ser gly ala leu thr ser gly val his thr phe pro
181
GCT GTC CTA CAG TCC TCA GGA CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC
ala val leu gln ser ser gly leu tyr ser leu ser ser val val thr val pro ser ser
201
AGC TTG GGC ACC CAG ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG
ser leu gly thr gln thr tyr ile cys asn val asn his lys pro ser asn thr lys val
221
GAC AAG AAA GTT GAG CCC AAA TCT TGT GAC AAA act aqt
asp lys lys val glu pro lys ser cys asp lys thr ser
231

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Fig. 2A

Human Antibody Sequence (TT sequence) (SEQ ID NO: 55)

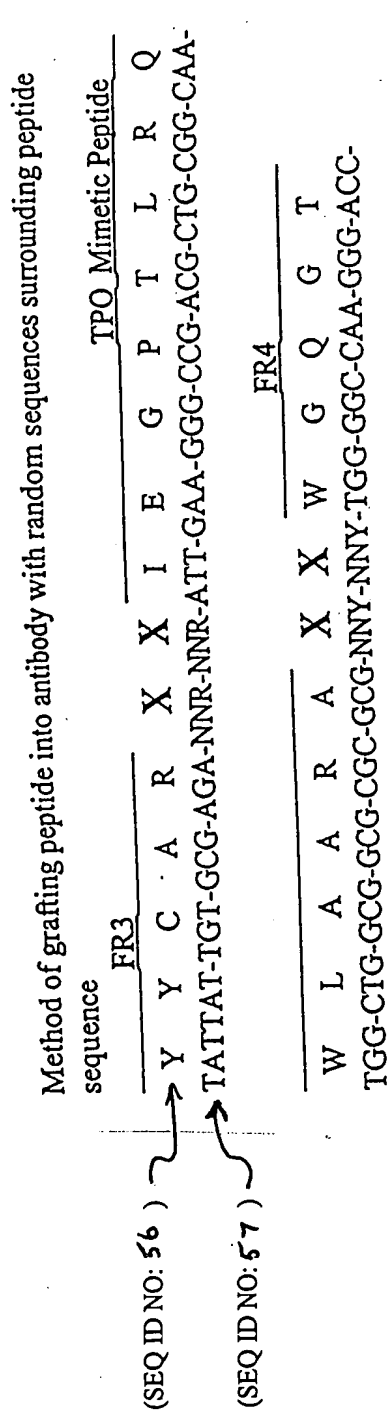
Light Chain: cloning sites Sac I and Xba I are underlined

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1      11
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glu leu thr gln ser pro gly thr leu ser leu ser pro gly glu arg ala thr leu ser
21      31
tgc agg gcc agt cac agt gtt agc agg gcc tac tta gcc tgg tac cag cag aaa cct ggc
cys arg ala ser his ser val ser arg ala tyr leu ala trp tyr gln gln lys pro gly
41      51
cag gct ccc agg ctc ctc atc tat ggt aca tcc agc agg gcc act ggc atc cca gac agg
gln ala pro arg leu leu ile tyr gly thr ser ser arg ala thr gly ile pro asp arg
61      71
ttc agt ggc agt ggg tct ggg aca gac ttc act ctc acc atc agc aga ctg gag cct gaa
phe ser gly ser gly ser gly thr asp phe thr leu thr ile ser arg leu glu pro glu
81      91
gat ttt gca gtg tac tac tgt cag cag tat ggt ggc tca ccg tgg ttc ggc caa ggg acc
asp phe ala val tyr tyr cys gln gln tyr gly gly ser pro trp phe gly gln gly thr
101     111
AAG GTG GAA CTC AAA CGA ACT GTG GCT GCA CCA TCT GTC TTC ATC TTC CCG CCA TCT GAT
lys val glu leu lys arg thr val ala ala pro ser val phe ile phe pro pro ser asp
121     131
GAG CAG TTG AAA TCT GGA ACT GCC TCT GTT GTG TGC CTG CTG AAT AAC TTC TAT CCC AGA
glu gln leu lys ser gly thr ala ser val val cys leu leu asn asn phe tyr pro arg
141     151
GAG GCC AAA GTA CAG TGG AAG GTG GAT AAC GCC CTC CAA TCG GGT AAC TCC CAG GAG AGT
glu ala lys val gln trp lys val asp asn ala leu gln ser gly asn ser gln glu ser
161     171
GTC ACA GAG CAG GAC AGC AAG GAC AGC ACC TAC AGC CTC AGC AGC ACC CTG ACG CTG AGC
val thr glu gln asp ser lys asp ser thr tyr ser leu ser ser thr leu thr leu ser
181     191
AAA GCA GAC TAC GAG AAA CAC AAA GTC TAC GCC TGC GAA GTC ACC CAT CAG GGC CTG AGC
lys ala asp tyr glu lys his lys val tyr ala cys glu val thr his gln gly leu ser
201     211
TTG CCC GTC ACA AAG AGC TTC AAC AGG GGA GAG TGT TAG Ttc taq a
leu pro val thr lys ser phe asn arg gly glu cys AMB

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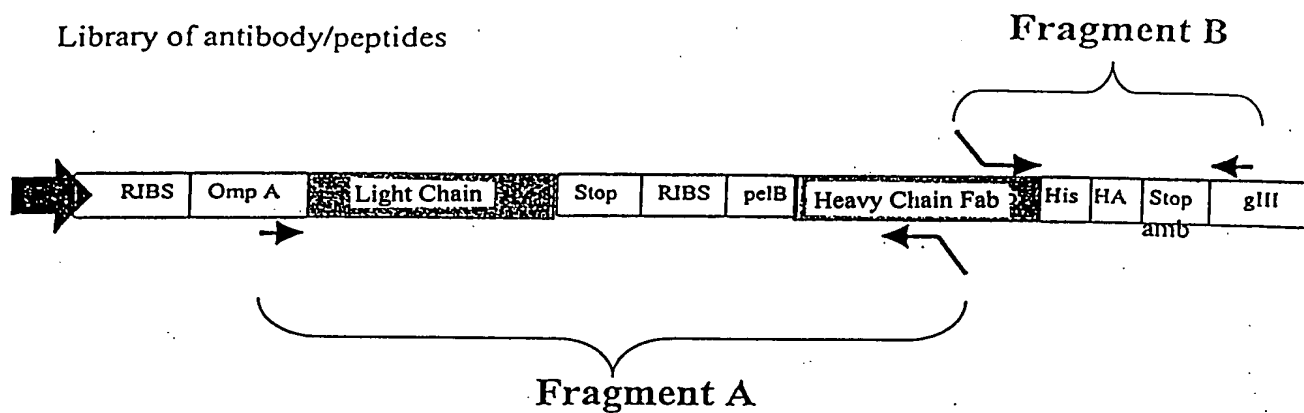
Fig. 2B



The TPO mimetic peptide was grafted into the heavy chain CDR3 region of the tetanus toxoid antibody. The peptide was flanked on either side by two random amino acids, shown as "X"s in the figure.

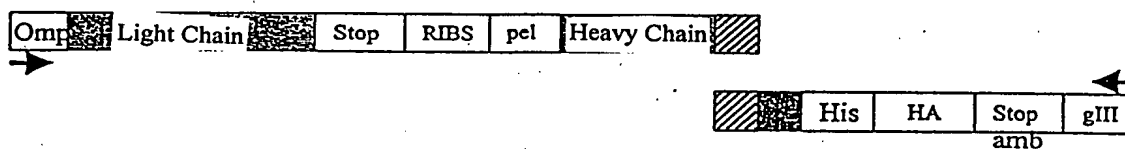
Fig. 3

Library of antibody/peptides



Fragment A

Fragment B



HCDR3 Library

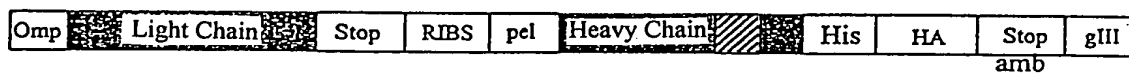


Fig. 4

<u>CLONE</u>	<u>AMINO ACID SEQUENCE</u>	<u>SEQ. ID NO.</u>
X1a	Pro-Pro-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Gly-Gly CCG-CCC-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-GGA-GGC	25 26
X1a-11	Gly-Gly-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Gly-Gly GGG-GGT-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-GGC-GGA	27 28
X1a-13	Gly-Gly-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Gly-Gly GGC-GGT-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-GGA-GGC	29 30
X1c	Trp-Leu-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Pro-Val TGG-CTG-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-CCT-GTC	31 32
X2c	Met-Ile-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Val-Gly ATG-ATA-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-GTT-GGC	33 34
X3a	Val-Val-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Pro-Val GTG-GTA-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-CCT-GTT	35 36
X3b	Gly-Pro-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Pro-Asp GGG-CCG-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-CCC-GAT	37 38
X4b	Leu-Pro-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Pro-Val TTG-CCA-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-CCT-GTT	39 40
X4c	Ser-Leu-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Pro-Ile TCA-CTG-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-CCC-ATC	41 42
X5a	Thr-Met-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Pro-Val ACA-ATG-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-CCC-GTT	43 44
X5c	Thr-Thr-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Pro-Val ACG-ACA-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-CCT-GTC	45 46
X7a	Thr-Arg-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Cys-Ser ACA-CGG-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-TGC-AGC	47 48
X7b	no peptide deletion mutant	
X7c	Gln-Thr-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Pro-Asp CAG-ACA-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-CCT-CAC	49 50

Fig. 5

pRL8

(SEQ ID NO: 60)

GGGAAATTGTAAGCGTTAATATTTTGTGTTAAAATTTCGCGTTAAATTTTGTGTTAA
ATCAGCTCATTTTTTAACCAATAGGCCGAAATCGGCAAAATCCCTTATAAATC
AAAAGAATAGACCGAGATAGGGTTGAGTGTTGTTCCAGTTTGGAAACAAGAGT
CCACTATTAAAGAACGTGGACTCCAACGTCAAAGGGCGAAAAACCGTCTATC
AGGGCGATGGCCCACTACGTGAACCATCACCTAATCAAGTTTTTTGGGGTC
GAGGTGCCGTAAAGCACTAAATCGGAACCCTAAAGGGAGCCCCCGATTAGAG
GCTTGACGGGGAAAGCCGGCGAACGTGGCGAGAAAGGAAGGGAAGAAAGC
GAAAGGAGCGGGCGCTAGGGCGCTGGCAAGTGTAAGCGGTCACGCTGCGCGT
AACCACCACACCCGCCGCGCTTAATGCGCCGCTACAGGGCGCGTCAGGTGGC
ACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTATTTTTCTAAATA
TTCAAATATGTATCCGCTCATGAGACAATAACCCTGATAAATGCTTCAATAAT
ATTGAAAAAGGAAGAGTATGAGTATTCAACATTTCCGTGTCGCCCTTATTCCC
TTTTTTGCGGCATTTTGCCTTCCTGTTTTTGTCTACCCAGAAACGCTGGTGAAA
GTAAAAGATGCTGAAGATCAGTTGGGTGCACGAGTGGGTTACATCGAACTGG
ATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAACGTTTTTCCA
ATGATGAGCACTTTTAAAGTTCTGCTATGTGGCGCGGTATTATCCCGTATTGA
CGCCGGGCAAGAGCAACTCGGTGCGCGCATACACTATTCTCAGAATGACTTG
GTTGAGTACTCACCAGTCACAGAAAAGCATCTTACGGATGGCATGACAGTAA
GAGAATTATGCAGTGCTGCCATAACCATGAGTGATAACACTGCGGCCAACTT
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ATGGGGGATCATGTAACTCGCCTTGATCGTTGGGAACCGGAGCTGAATGAAG
CCATACCAAACGACGAGCTGTACACCACGATGCCTGTAGCAATGGCAACAAC
GTTGCGCAAACTATTAAGTGGCGAACTACTTACTCTAGCTTCCCGGCAACAAT
TAATAGACTGGATGGAGGCGGATAAAGTTGCAGGACCACTTCTGCGCTCGGC
CCTTCCGGCTGGCTGGTTTTATTGCTGATAAATCTGGAGCCGGTGAGCGTGGGT
CTCGCGGTATCATTGCAGCACTGGGGCCAGATGGTAAGCCCTCCCGTATCGT
AGTTATCTACACGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACA
GATCGCTGAGATAGGTGCCTCACTGATTAAGCAATTGGTAAGTGTACAGACCAA
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ATCTAGGTGAAGATCCTTTTTGATAATCTCATGACCAAAATCCCTTAACGTGA
GTTTTTCGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGATCTTCTT
GAGATCCTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAAACCACCG
CTACCAGCGGTGGTTTTGTTTGGCGGATCAAGAGCTACCAACTCTTTTTCCGAA
GGTAAGTGGCTTCAGCAGAGCGCAGATACCAAATACTGTCCTTCTAGTGTAAG
CCGTAGTTAGGCCACCACTTCAAGAACTCTGTAGCACCGCCTACATACTCGC
TCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTGTCTTA
CCGGGTTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTCCGGGCTG
AACGGGGGGTTCGTGCACACAGCCAGCTTGGAGCGAACGACCTACACCGA

Fig. 6A

10006593.120501

ACTGAGATACCTACAGCGTGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGG
 AGAAAGGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACAGGAGAGCGC
 ACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTATAGTCCTGTCCGGT
 TTCGCCACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCGG
 AGCCTATGGAAAAACGCCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTG
 CTGGCCTTTTGCTCACATGTTCTTTCTGCGTTATCCCCTGATTCTGTGGATAA
 CCGTATTACCGCCTTTGAGTGAGCTGATACCGCTCGCCGCAGCCGAACGACC
 GAGCGCAGCGAGTCAGTGAGCGAGGAAGCGGAAGAGCGCCCAATACGCAAA
 CCGCCTCTCCCCGCGCGTTGGCCGATTCATTAATGCAGCTGGCACGACAGGTT
 TCCCGACTGGAAAGCGGGCAGTGAGCGCAACGCAATTAATGTGAGTTAGCTC
 ACTCATTAGGCACCCCAGGCTTTACACTTTATGCTTCCGGCTCGTATGTTGTG
 TGGAATTGTGAGCGGATAACAATTGAATTCAGGAGGAATTTAAAATGAAAAA
 GACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCTACCGTGGCCCGAG
 GCGGCCGAGCTCGGCCATGGCTGGTTGGGCAGCGAGTAATAACAATCCAGCG
 GCTGCCGTAGGCAATAGGTATTTCAATTATGACTGTCTCCTTGGCGACTAGCTA
 GTTTAGAATTTCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCC
 GCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGTAAGCCTGG
 GGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGC
 TTTCAGTCGGGAAACCTGTCTGTACTAATGATGGTGATGGTGATGGCTAG
 TTTTGTGACAAGATTTGGGCTCAACTTCTTGTCACCTTGGTGTTGCTGGGCT
 TGTGATTACGTTGCAGATGTAGGTCTGGGTGCCCAAGCTGCTGGAGGGCAC
 GGTCACCACGCTGCTGAgGGAGTAGAGTCCTGAGGACTGTAGGACAGCCGGG
 AAGGTGTGCACGCCGCTGGTCAgGGCGCCTGAgTTCCACGACACcGTCGCCGG
 TTCgGGGAAGTAGTCCTTGACCAGGCAGCCAGGGCCGCTGTGCCCCCAGAG
 GTGCTCTTGAGGAGGGGTGCCAGGGGGAAGACCGATGGGCCCTTGGTGAG
 GCTGCGGAGACGGTGACCGTGGTACCAGCAGAAACCTGGCCAGGCTCCCAG
 GCTCCTCATCTATGGTACATCCAGCAGGGCCACTGGCATCCCAGACAGGTTT
 AGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGC
 CTGAAGATTTTGCAGTGTACTACTGTGTCAGCAGTATGGTGGCTCACCGTGGTTC
 GGCCAAGGGACCAAGGTGGAACCTCAAACGAACTGTGGCTGCACCATCTGTCT
 TCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTG
 TGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGG
 ATAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAGGACAG
 CAAGGACAGCACCTACAGCCTCAGCAGCACCCCTGACGCTGAGCAAAGCAGA
 CTACGAGAAACACAAAGTCTACGCCTGCGAAGTCacccatcagggectgagltcgccgtcac
 aaagagcttcaacggaggagagtgttaatTCTAGATAATTAATTAGGAGGAATTTAAAATGAA
 ATACCTATTGCCTACGGCAGCCGCTGGATTGTTATTACTCGCTGCCCAACCAG
 CCATGGCCGAGGTGCAGCTGCTCGAGATGAGCGATAAAATTATTCACCTGAC
 TGACGACAGTTTTGACACGGATGTACTCAAAGCGGACGGGGCGATCCTCGTC
 GATTTCTGGGCAGAGTGGTGCGGTCCGTGCAAAATGATCGCCCCGATTCTGG
 ATGAAATCGCTGACGAATATCAGGGCAAACCTGACCGTTGCAAACTGAACAT
 CGATCAAAACCCTGGCACTGCGCCGAAATATGGCATCCGTGGTATCCCGACT
 CTGCTGCTGTTCAAAAACGGTGAAGTGGCGGCAACCAAAGTGGGTGCACTTG
 TCTAAAGGTCAGTTGAAAGAGTTCCTCGACGCTAACCTGGCGTACCCGTACG
 ACGTTCCGGACTACGGTTCTACTAGTccgaaccgtctacccacggggtcttctcggtggccgc
 atcgcccgctcgaggaaaaagtgaaaccctgaaagctcagaactccgagctggcgctccactgccaacatgctgcgcgaac

Fig. 6B

aggtggcacagctgaaacagaaagtattgaaccatggcggltgtgctagtGCCAGGCCGGCCAGCACCAT
CACCATCACCATGGCGCATACCCGTACGACGTTCCGGACTACGCTTCTTAGG
AGGGTGGTGGCTCTGAGGGTGGCGGTTCTGAGGGTGGCGGCTCTGAGGGAGG
CGGTTCCGGTGGTGGCTCTGGTTCCGGTGATTTTGATTATGAAAAGATGGCAA
ACGCTAATAAGGGGGCTATGACCGAAAATGCCGATGAAAACGCGCTACAGTC
TGACGCTAAAGGCAAACCTTGATTCTGTGCTACTGATTACGGTGCTGCTATCG
ATGGTTTCAATTGGTGACGTTTCCGGCCTTGCTAATGGTAATGGTGCTACTGGT
GATTTTGCTGGCTCTAATTCCCAAATGGCTCAAGTCGGTGACGGTGATAATTC
ACCTTTAATGAATAATTTCCGTCAATATTTACCTTCCCTCCCTCAATCGGTTGA
ATGTCGCCCTTTTGTCTTTAGCGCTGGTAAACCATATGAATTTTCTATTGATTG
TGACAAAATAAACTTATTCCGTGGTGTCTTTGCGTTTCTTTTATATGTTGCCAC
CTTTATGTATGTATTTTCTACGTTTGCTAACATACTGCGTAATAAGGAGTCTTA
AGCTAGCTAATTAATTTAAGCGGCCGCAGATCT

Fig. 6C

pRL8

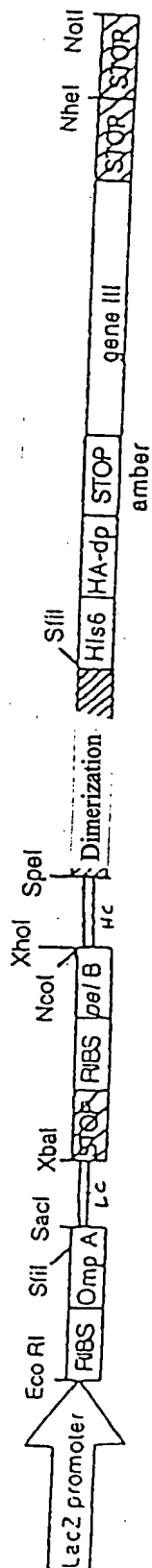


Fig. 7

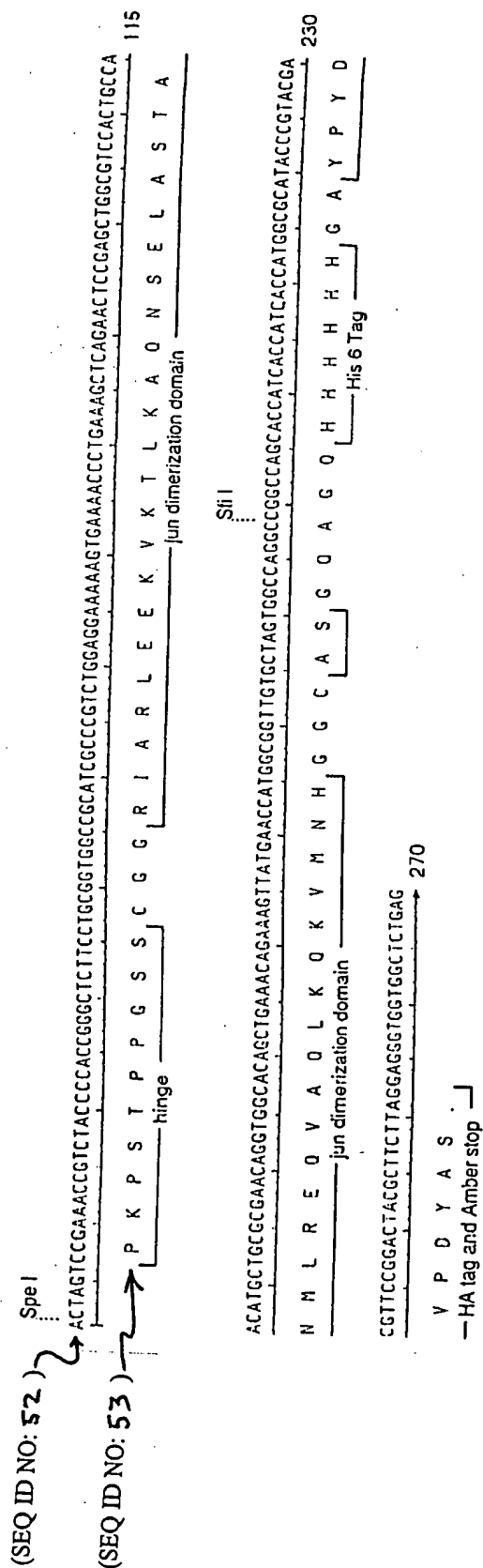


Fig. 8

TPO Positive Clones nnk nnk nnk nnk
 1 2 IEGPTLRQWLAARA 3 4

	Sample	nnk	nnk	nnk	nnk	Amino Acids		Amino Acids	
		1	2	3	4	1	2	3	4
HC CDR3	X1c	tgg	ctg	cct	gtc	Trp	Leu	Pro	Val
	X3a	gtg	gta	cct	gtt	Val	Val	Pro	Val
	X3b	ggg	ccg	ccc	gat	Gly	Pro	Pro	Asp
	X4b	ttg	cca	cct	gtt	Leu	Pro	Pro	Val
	X4c	tca	ctg	ccc	atc	Ser	Leu	Pro	Ile
	X5a	aca	atg	ccc	gtt	Thr	Met	Pro	Val
	X5c	acg	aca	cct	gtc	Trp	Leu	Pro	Val
HC CDR2	X7c	cag	aca	cct	cac	Gln	Thr	Pro	Asp
	24	ctt	tat	tct	aat	Leu	Tyr	Ser	Asn
	39	act	tac	ttg	cat	Thr	Tyr	Leu	His
	3	agg	atg	ctc	gag	Arg	Met	Leu	Glu
	7	aag	gaa	tct	aag	Lys	Glu	Ser	Lys
	8	gcg	cat	gtg	cag	Ala	His	Val	Gln
	10	cag	gag	att	agt	Gln	Glu	Ile	Ser
	11	cgg	aat	aat	ccg	Arg	Asn	Asn	Pro
	19	cag	cta	aat	tct	Gln	Leu	Asn	Ser
	25	agt	att	ttt	gtc	Ser	Ile	Phe	Val
	28	ggg	ccc	act	agt	Gly	Pro	Thr	Ser
	10	aag	ggt	gtt	agt	Lys	Gly	Val	Ser
LC CDR1	11	cat	ggg	gtg	gct	His	Gly	Val	Ala
	12a	cgt	acg	atg	gct	Arg	Thr	Met	Ala
	12b	cgt	ggt	gtt	aat	Arg	Gly	Val	Asn
	14	cgt	tcg	ctt	gcg	Arg	Ser	Leu	Ala
	16	cgg	ggt	gtt	gcg	Arg	Gly	Val	Ala
	18	agg	acg	gtg	tct	Arg	Thr	Val	Ser
	47	aag	ggg	gtg	gcg	Lys	Gly	Val	Ala
LC CDR2	1	aat	ccg	agg	ggt	Asn	Pro	Arg	Gly
	2	tcg	cct	cgg	agt	Ser	Pro	Arg	Ser
	3	tcg	cct	cgt	acg	Ser	Pro	Arg	Thr
	4	tcg	cct	tgg	cgt	Ser	Pro	Trp	Arg
	5	act	ccg	aat	tgg	Thr	Pro	Asn	Trp
	6	aat	cct	gcg	agg	Asn	Pro	Ala	Arg
	7	aat	ccg	tcg	ggg	Asn	Pro	Ser	Gly
	9	aat	cct	tat	tag	Asn	Pro	Tyr	Stop
	10	aat	ccg	cgg	tct	Asn	Pro	Arg	Ser
	11	aat	ccg	gat	gtg	Asn	Pro	Asp	Val
	12	tcg	ccg	tcg	cgg	Ser	Pro	Ser	Arg
	13	aat	cct	ctg	ttt	Asn	Pro	Leu	Phe
	14	aat	ctt	ggg	tat	Asn	Pro	Gly	Tyr
	15	aat	cct	att	agt	Asn	Pro	Ile	Ser
	16	aat	cct	cag	cgg	Asn	Pro	Gln	Arg
	18	aat	ccg	cgg	acg	Asn	Pro	Arg	Thr
	19	aat	ccg	cgt	ggg	Asn	Pro	Arg	Gly
	20	cat	ttg	aga	ctg	His	Leu	Arg	Leu
	21	aag	tag	att	tat	Lys	Stop	Ile	Tyr
	23	aat	cct	ggt	aag	Asn	Pro	Gly	Lys
	24	aat	cct	cgt	ggg	Asn	Pro	Arg	Gly
	26	aat	cct	aat	gtg	Asn	Pro	Asn	Val
	27	tct	ccg	cgg	gtt	Ser	Pro	Arg	Val
	29	acg	cct	cgg	ggt	Thr	Pro	Arg	Gly
	30	cct	tag	tgg	tgg	Pro	Stop	Trp	Trp

FIG. 9

40006593.120504

Activity of Fab clones containing 2 TPO mimetic peptides

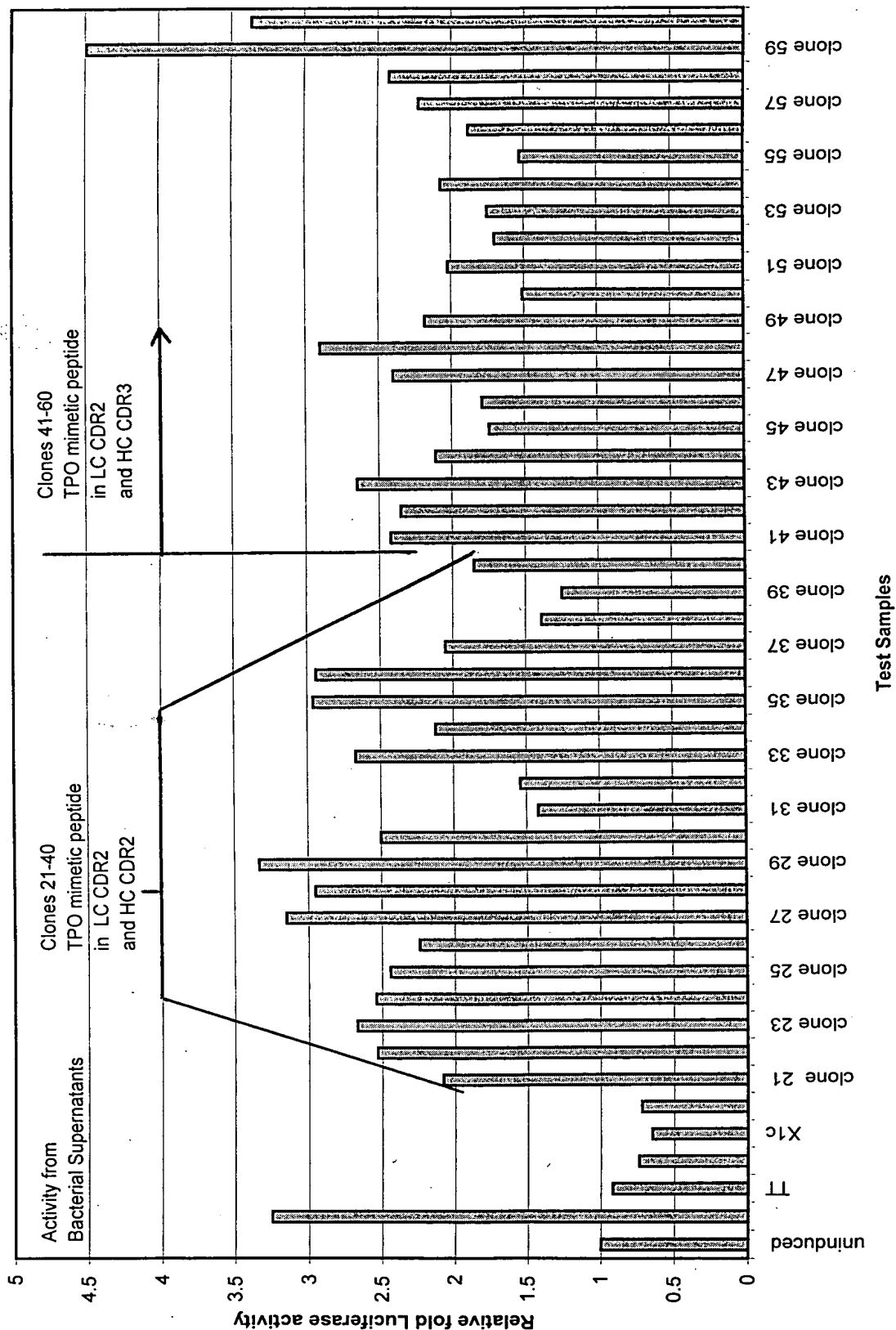


FIGURE 10

Activity of Fab clones containing 2 or 3 TPO mimetic peptides

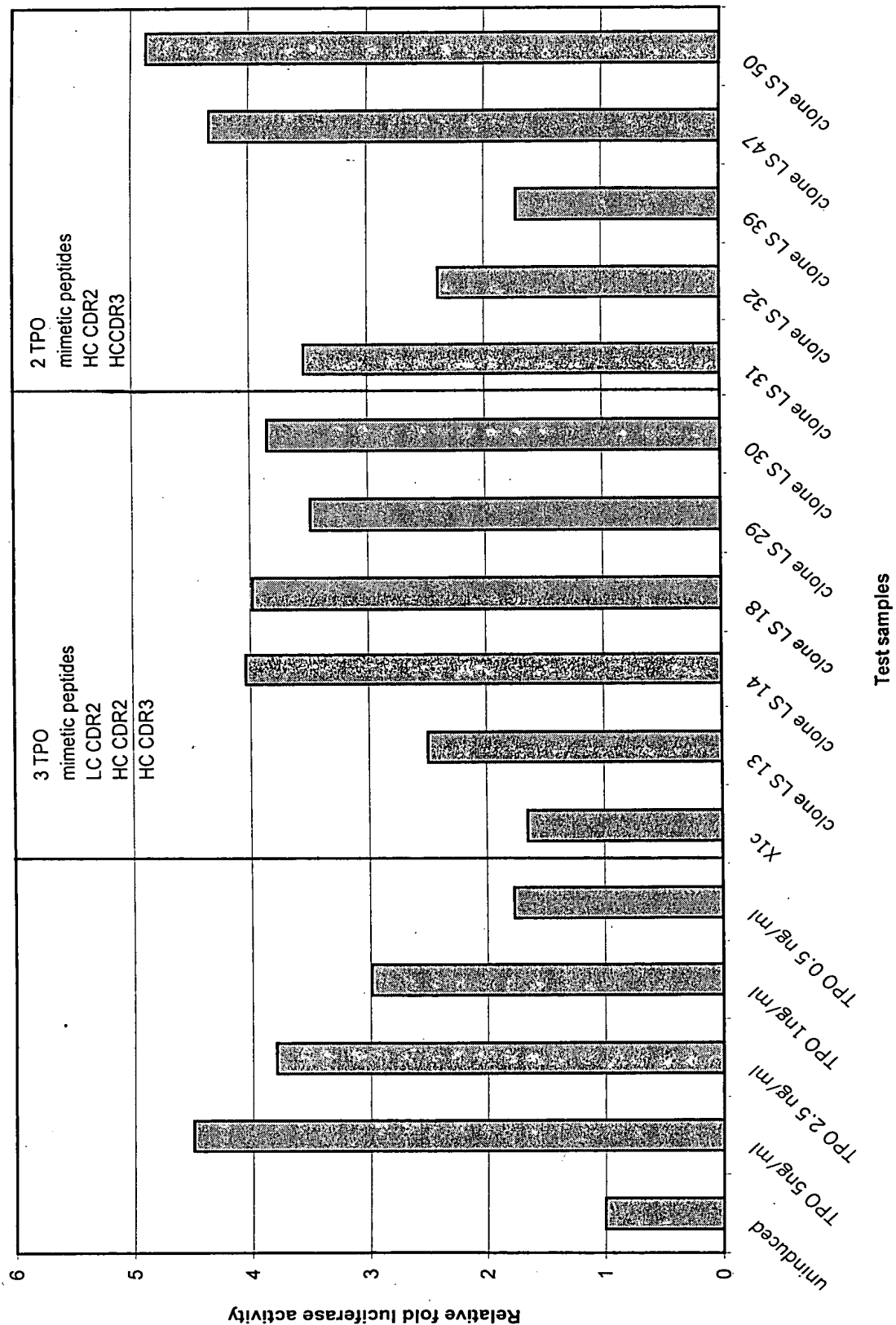


FIGURE 11

TPO Mimetic Activity of semi-purified Fab clone 59

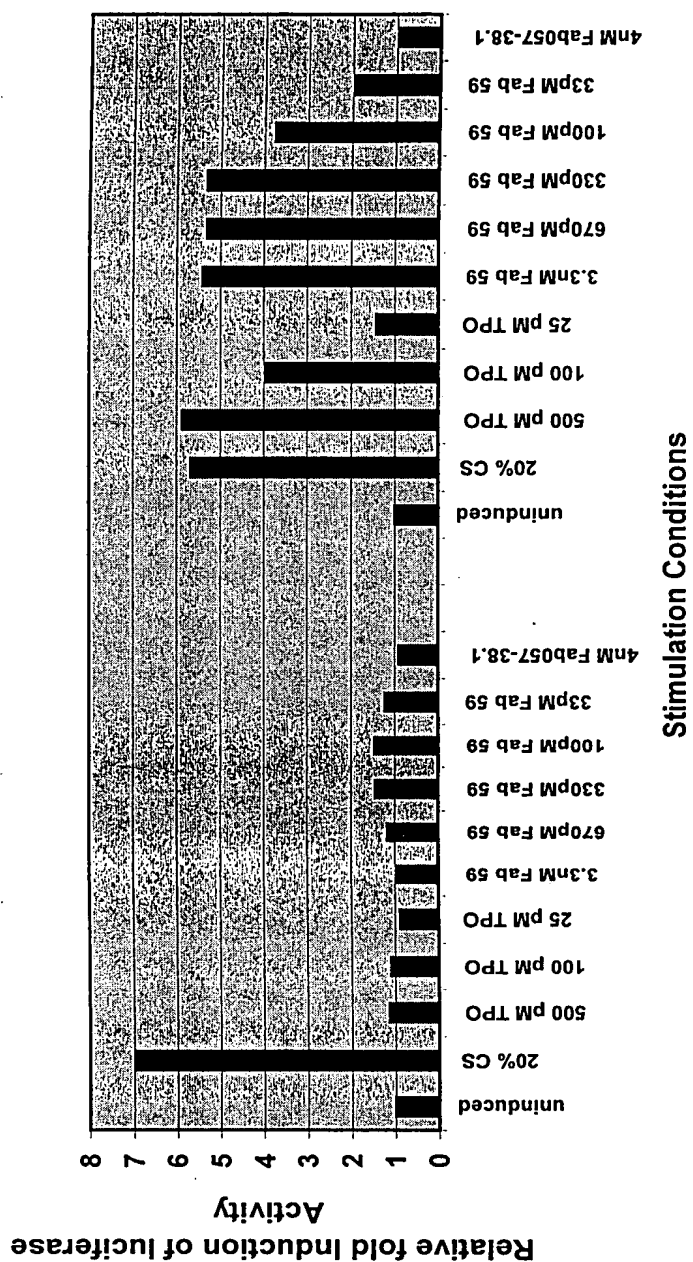


Fig. 12

(SEQ ID NO: 67)

5G1.1 – TPO Heavy Chain (Bold denotes TPO mimetic) Amino acid sequence:

MKIVSWVILFLLSVTAGVHSQVQLVQSGAEVKKPGASVKVSCKASGYIFSNIYWIQW
VRQAPGQGLEWMGEILPGSGSTEYTENFKDRVTMTRDTSTSTVYMELSSLRSED
TAVYYCARLPIEGPTLRQWLAARAPVWGQGLTVTVSSASTKGPSVFPLAPCSR
STSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTV
PSSNFGTQTYTCNVDHKPSNTKVDKTVERKCCVECPAPPVAGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQ
EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRL
TVDKSRWQEGNVFSCSVMHENHYTQKSLSLSLGK.

(SEQ ID NO: 68)

5G1.1 – TPO Heavy Chain (Bold denotes TPO mimetic) Nucleic acid sequence:

ATGAAGTGGAGCTGGGTTATTCTCTTCTCCTGTCAGTAAGTCCCGGCGTCCA
CTCCCAAGTCCAAGTGGTGCAATCCGGCGCCGAGGTCAAGAAGCCAGGGGCC
TCAGTCAAAGTGTCCTGTAAAGCTAGCGGCTATATTTTTTCTAATTATTGGAT
TCAATGGGTGCGTCAGGCCCGGGCAGGGCCTGGAATGGATGGGTGAGATC
TTACCGGGCTCTGGTAGCACCGAATATACCGAAAATTTTAAAGACCGTGTTA
CTATGACGCGTGACACTTCGACTAGTACAGTATACATGGAGCTCTCCAGCCTG
CGATCGGAGGACACGGCCGTCTATTATTGCGCGCGTTTGCCAATTGAAGGG
CCGACGCTGCGGCAATGGCTGGCGGGCGCGCGCGCCTGTTTGGGGTCAAG
GAACCCTGGTCACTGTCTCGAGCGCCTCCACCAAGGGCCCATCCGTCTTCCCC
CTGGCGCCCTGCTCCAGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTGCC
TGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAAGTCAAGCGC
CCTGACCAGCGGCGTGACACCTTCCCGGCTGTCCTACAGTCTCAGGACTCT
ACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAACTTCGGCACCCAGAC
CTACACCTGCAACGTAGATCACAAGCCAGCAACACCAAGGTGGACAAGAC
AGTTGAGCGCAAATGTTGTGTGTCGAGTGCCCAACCGTGCCAGCACCTGTG
GCAGGACCGTCAGTCTTCTCTTCCCCCAAACCAAGGACACCTCATGAT
CTCCCGGACCCCTGAGGTACGTGCGTGGTGGTGGACGTGAGCCAGGAAGAC
CCCGAGGTCCAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCATAATGCCA
AGACAAAGCCGCGGGAGGAGCAGTTCAACAGCACGTACCGTGTGGTCAGCG
TCCTCACCCTCCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA
GGTCTCCAACAAAGGCCTCCCGTCTCCATCGAGAAAACCATCTCCAAGCC
AAAGGGCAGCCCCGAGAGCCACAGGTGTACACCCTGCCCCCATCCCAGGAG
GAGATGACCAAGAACCAGGTACGCTGACCTGCCTGGTCAAAGGCTTCTACC
CCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAAC
ACAAGACCACGCCTCCCGTGTGGACTCCGACGGCTCCTTCTTCTCTACAGC
AGGCTAACCGTGGACAAGAGCAGGTGGCAGGAGGGGAATGTCTTCTCATGCT
CCGTGATGCATGAGGCTCTGCACAACCACTACACACAGAAGAGCCTCTCCCT
GTCTCTGGGTAAATGA

Fig. 13A

(SEQ ID NO: 69)

5G1.1 Light Chain Amino Acid Sequence

*MDMRVPAQLLGLLLWLRG*ARCDIQMTQSPSSLSASVGDRTITCGASENIYGALN
WYQQKPGKAPKLLIYGATNLADGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQ
NVLNTPITFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAK
VQWKVDNALQSGNSQESVTEQDSKDSSTLSKADYEEKHKVYACEVTH
QGLSSPVTKSFNRGEC.

(SEQ ID NO: 70)

5G1.1 Light Chain Nucleic Acid Sequence

ATGGACATGAGGGTCCCCGCTCAGCTCCTGGGGCTCCTGCTACTCTGGCTCCG
AGGTGCCAGATGTGATATCCAGATGACCCAGTCCCCGTCTCCCTGTCCGCCT
CTGTGGGCGATAGGGTCACCATCACCTGCGGCGCCAGCGAAAACATCTATGG
CGCGCTGAACTGGTATCAACAGAAACCCGGGAAAGCTCCGAAGCTTCTGATT
TACGGTGCGACGAACCTGGCAGATGGAGTCCCTTCTCGCTTCTCTGGATCCGG
CTCCGGAACGGATTTCACTCTGACCATCAGCAGTCTGCAGCCTGAAGACTTC
GCTACGTATTACTGTCAGAACGTTTTAAATACTCCGTTGACTTTTCGGACAGGG
TACCAAGGTGGAAATAAAACGAACCTGTGGCTGCACCATCTGTCTTCATCTTCC
CGCCATCTGATGAGCAGTTGAAATCTGGAAGTGCCTCTGTTGTGTGCCTGCTG
AATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCC
TCCAATCGGGTAACTCCCAGGAGAGTGTACAGAGCAGGACAGCAAGGACA
GCACCTACAGCCTCAGCAGCACCTGACGCTGAGCAAAGCAGACTACGAGA
AACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGT
CACAAAGAGCTTCAACAGGGGAGAGTGTTAG

Note: Italics denotes leader sequence

Fig. 13B

FACS staining on transfected 293 cells

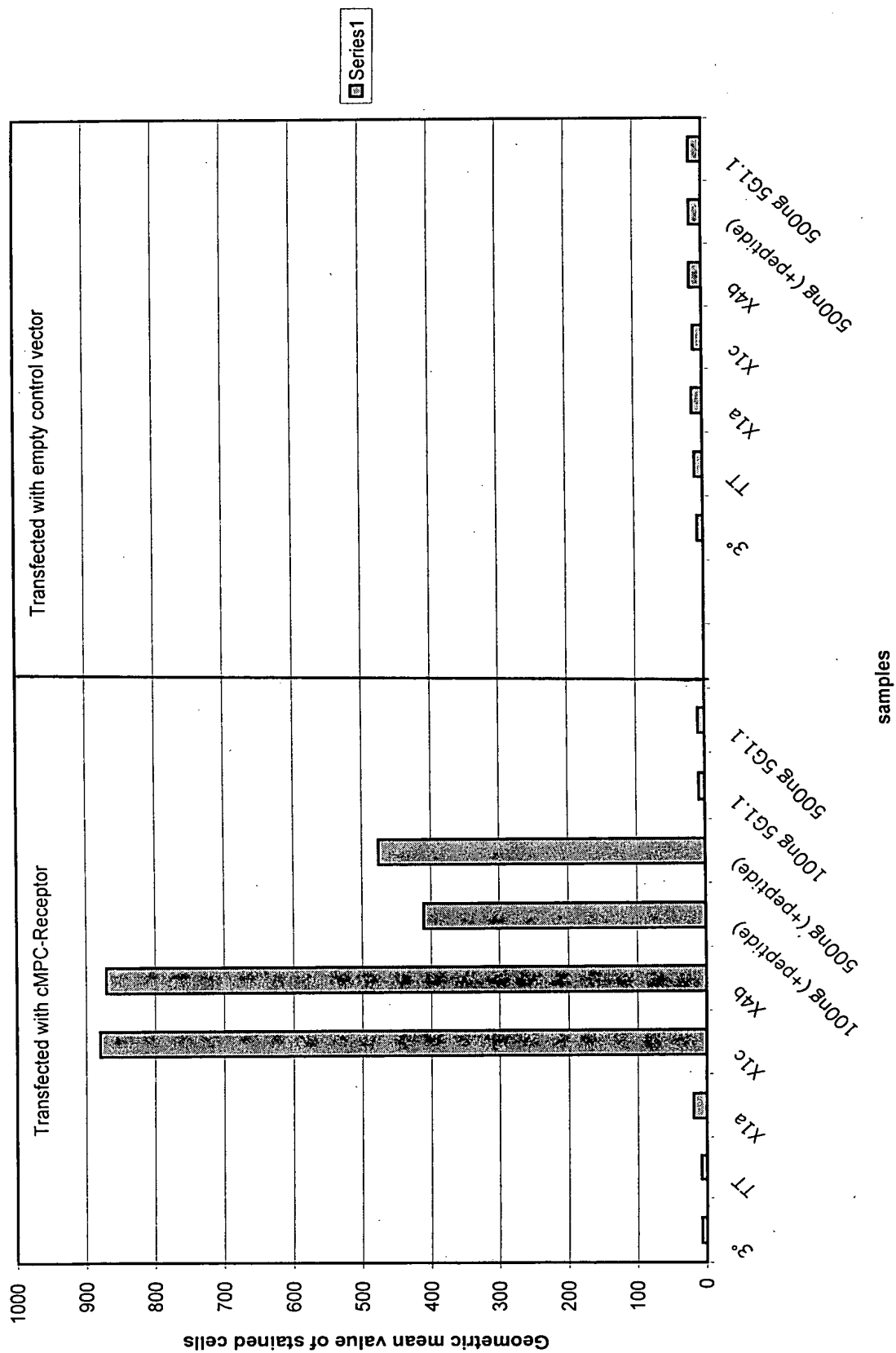


FIGURE 14

Activity of 5G1.1 containing the TPO mimetic Peptide

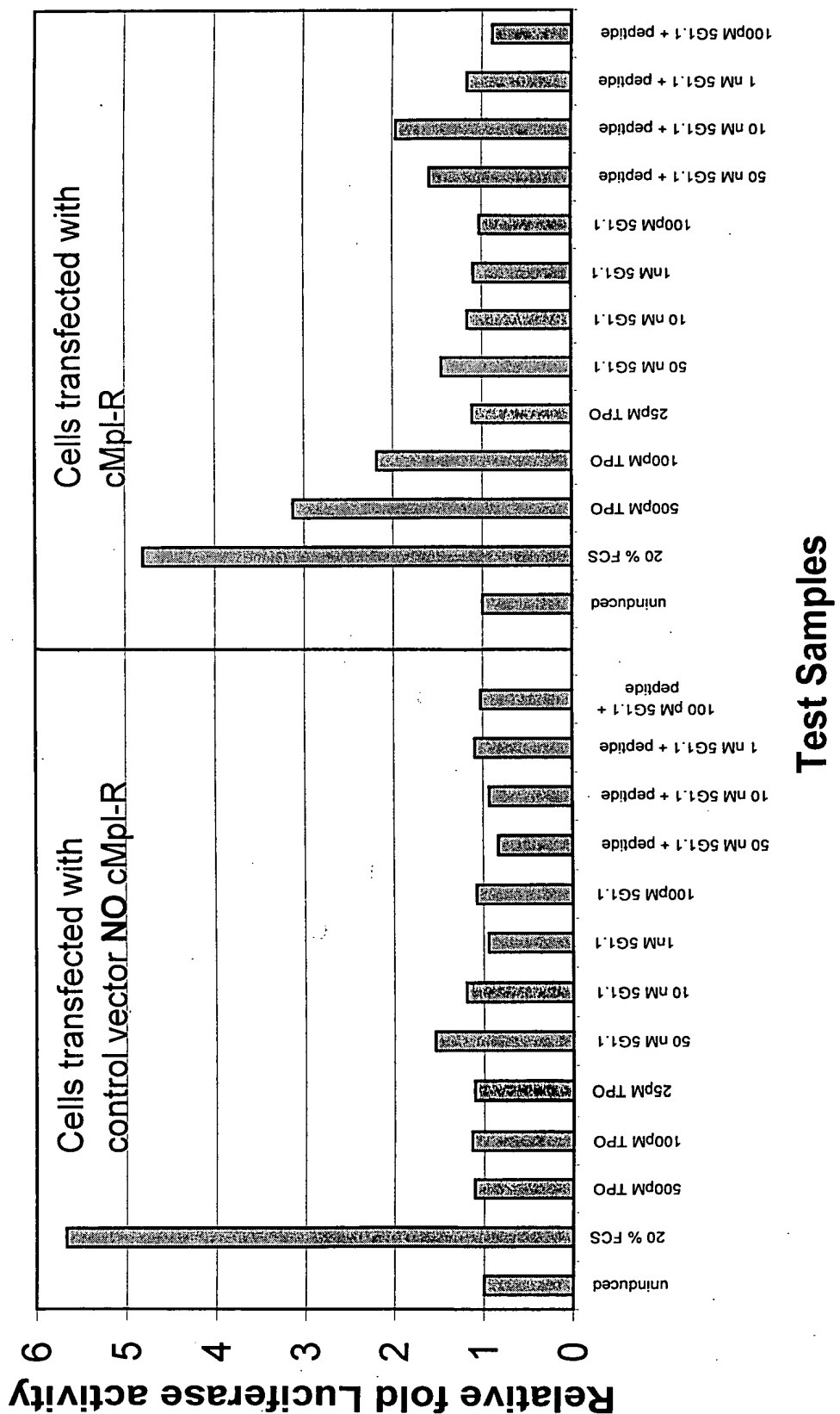


FIGURE 15

VARIABLE REGION OF 4-29 LIGHT CHAIN

(SEQ ID NO: 116)

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 27a 27b 27c 27d 27e 27f 28
GAC ATC CAG ATG ACC CAG TCT CCA TCC TCC CTG TCT GCA TCT GTA GGA GAC AGA GTC ACC ATC ACT TGC CGG GCG AGT CAG AGT

CDR1

CDR1

29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 52a 52b 52c 52d 52e 52f 52g 52h 52i 52j
ATT AGT AGT TTG CTG GCC TGG TAT CAG CAG AAA CCA GGG AAA GCT CCT AAG CTC CTG ATC TAT AAC CCG ATC GAA GGC CCA ACC CTG CGC CAG TGG CTG GCT

Grafted CDR2

Grafted CDR2

52k 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85
ACT CGC GCT CGT GGT GGG GTC CCA TCA AGG TTC AGC GGC AGT GGA TCT GGG ACA GAT TTC ACT CTC ACC ATC AGC AGC CTG CAG CCT GAA GAT TTT GCA ACT

CDR3

86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107
TAT TAC TGC CAA CAG TAT AAT AGT TAC CCT CCC ACT TTC GGC CCT GGC ACC AAA GTG GAT ATC AAA

Fig. 16

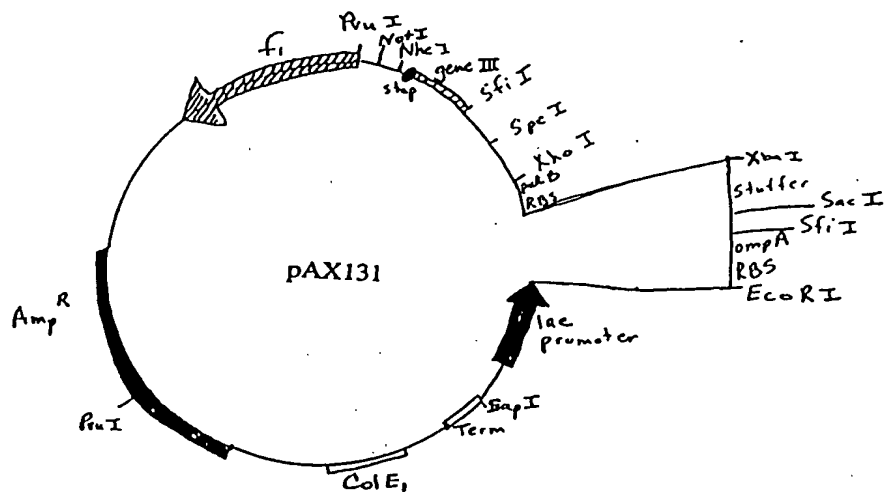
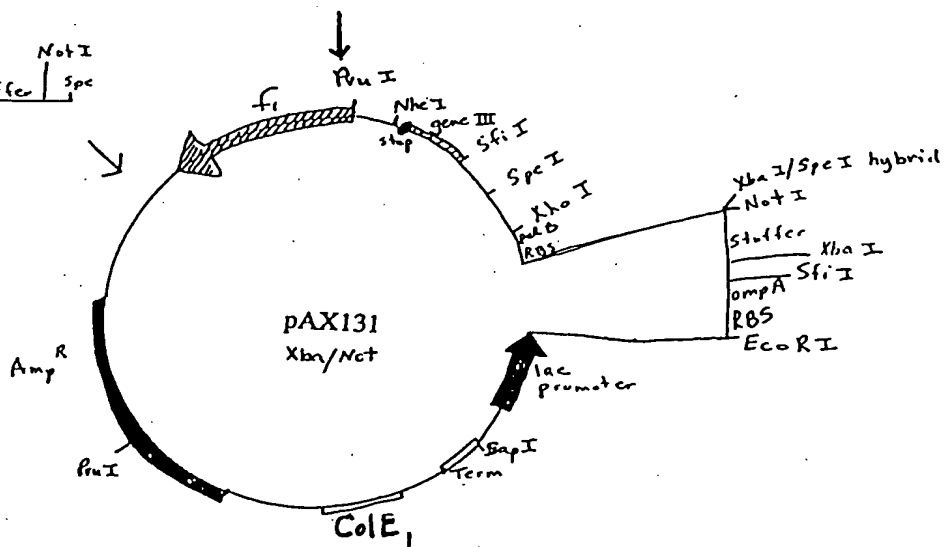
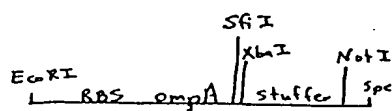
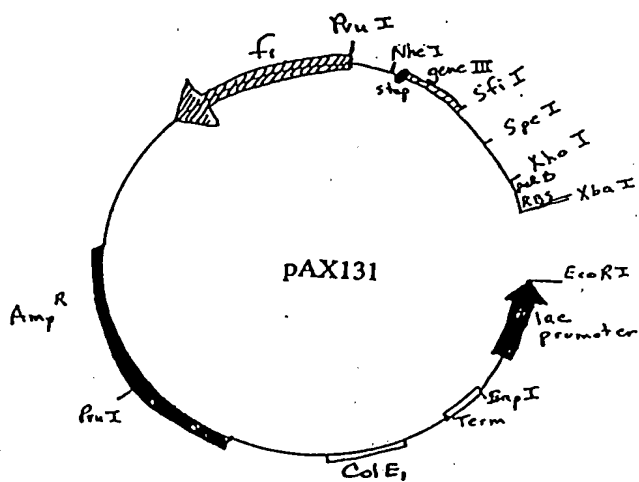


Fig. 17

1. Remove Not I site
2. digest with EcoRI and XbaI



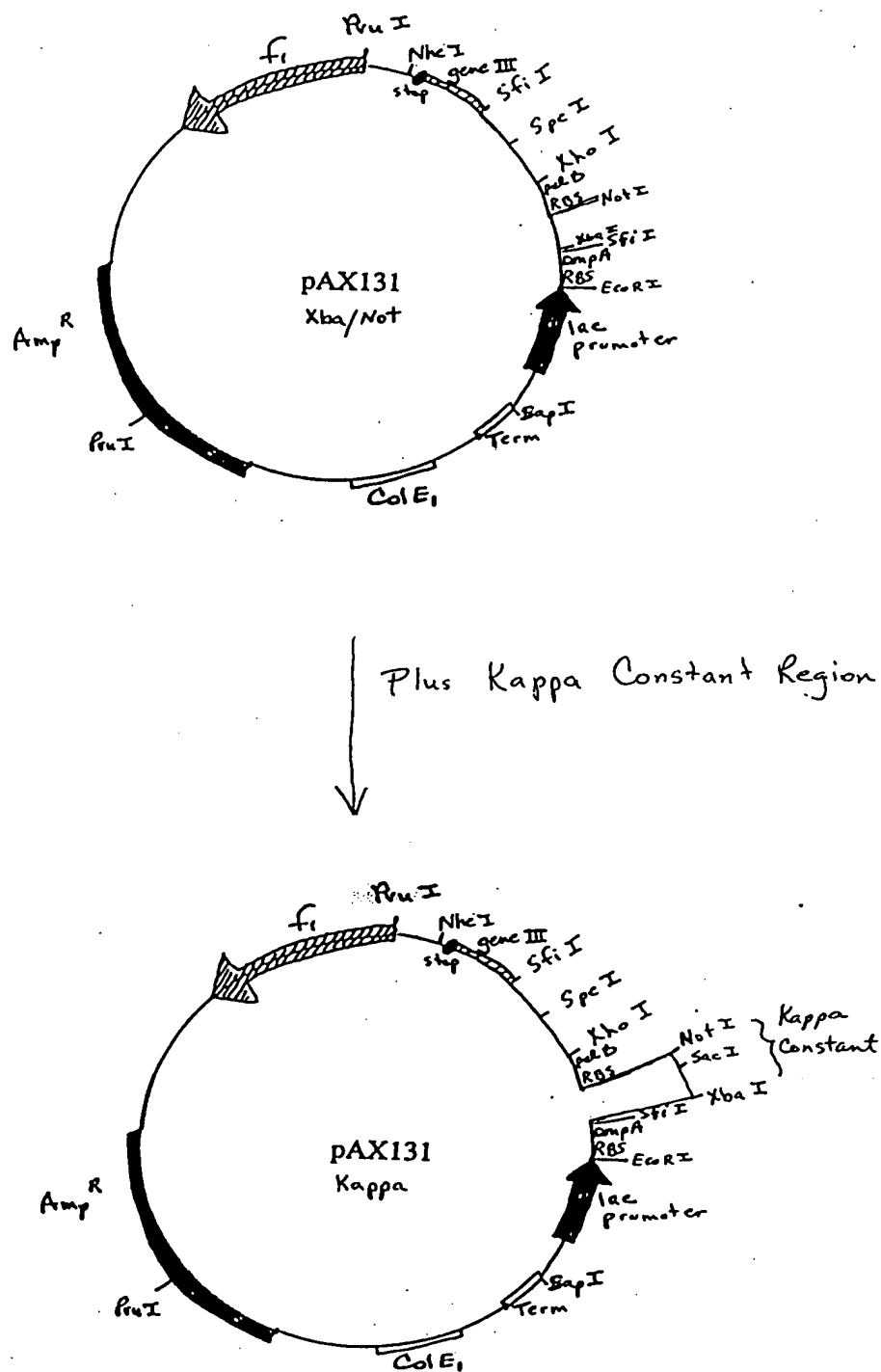


Fig. 18

10006593.120501

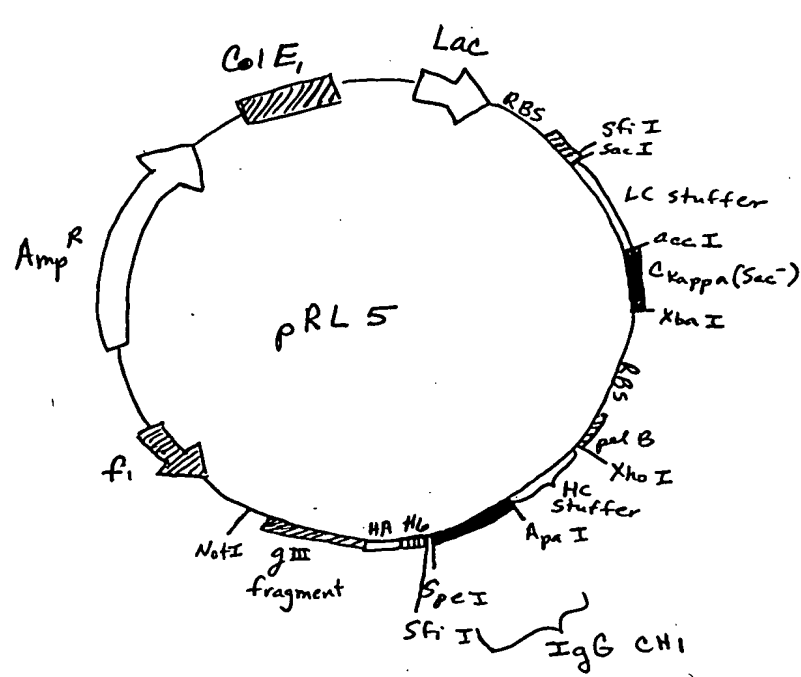


Fig. 19

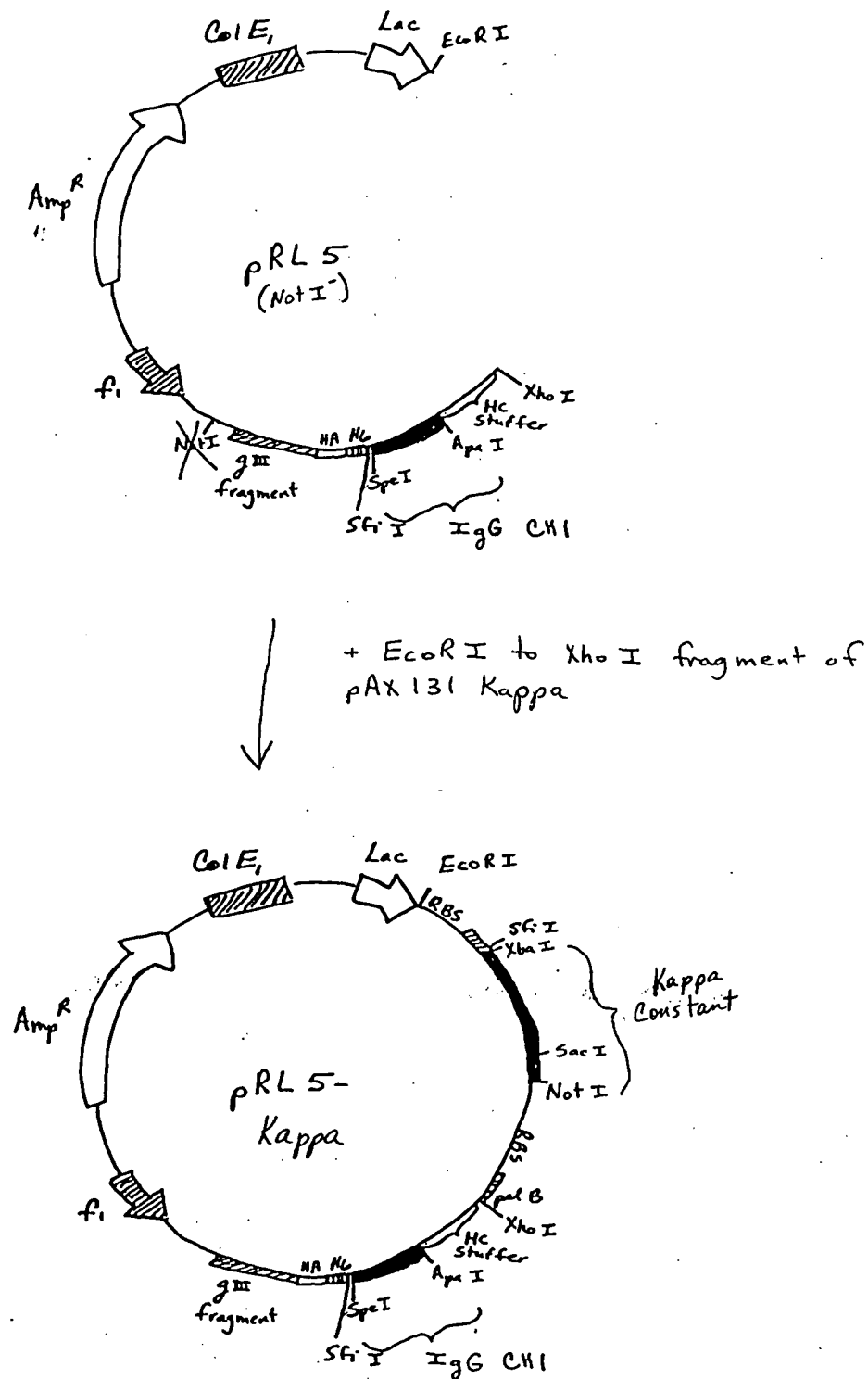


Fig. 20

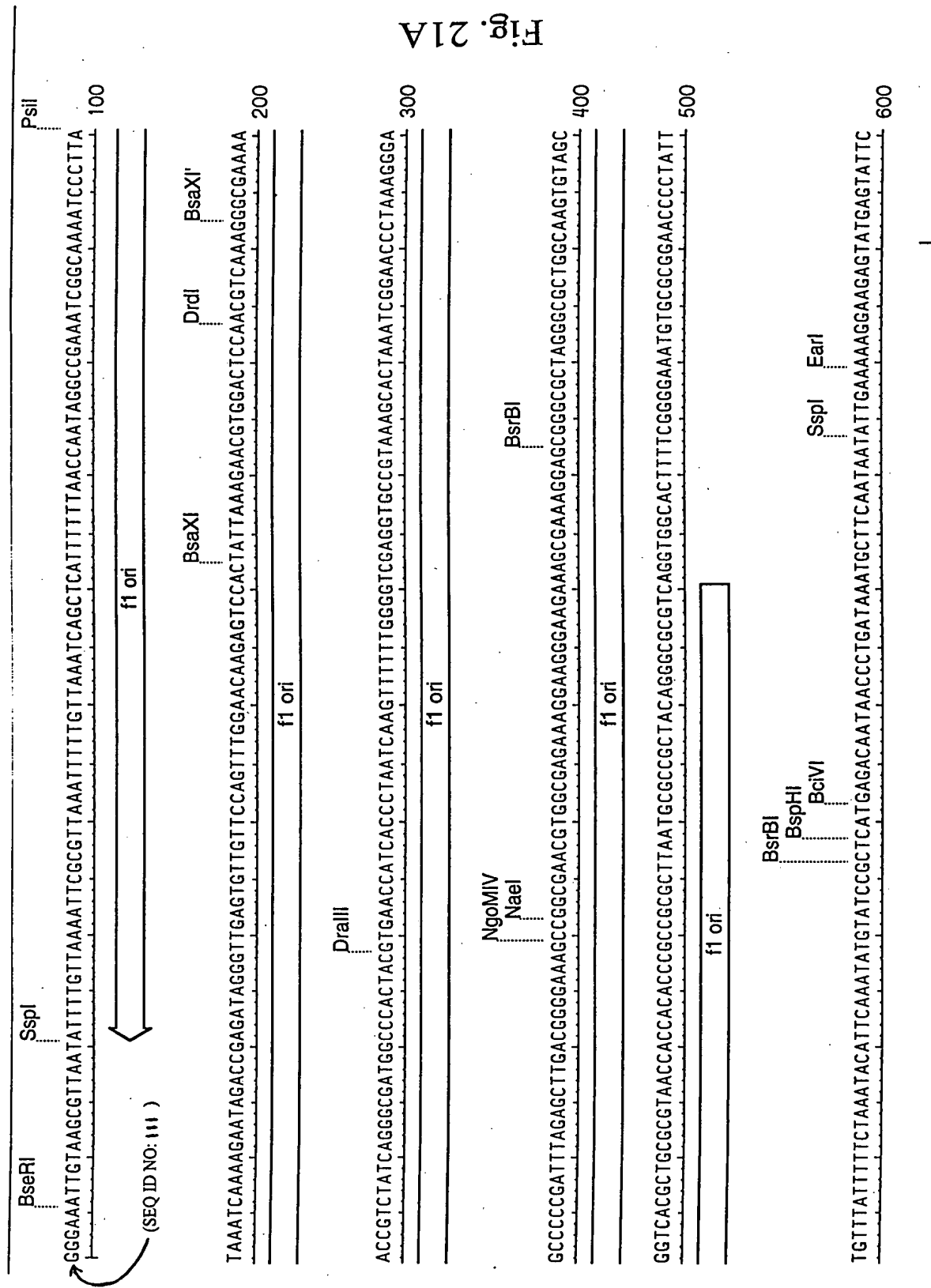


Fig. 21A

AACATTCGGTGGCCCTATTCCTTTTGGCGCATTTTGGCTTCCCTGTTTTGGCTACCCAGAAACGGCTGGGAAAGTAAAGATGCTGAAGATCA 700

beta-lactamase

GTGGGTGCACGAGTGGTTACATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAACGTTTTCCAATGATGAGCACITTT 800

ApaLI
BssSI
Eco57I

AclI
XmnI

DraI

beta-lactamase

AAAGTTCTGCTATGTGGCCGGTATTATCCCGTATTGACGCCGGCAAGAGCAACTCGGTGCGCCGCATACACTATTCAGAAATGACTTGGTTGAGTACT 900

BcgI

BcgI

Scal

beta-lactamase

CACCAGTCACAGAAAAGCATCTTACGGATGGCATGACAGTAAGAGAATTATGCAGTGTGCCATAACCATGAGTGATAACACTGCGGCCAACTTACTTCT 1000

BtsI

BtsI

beta-lactamase

GACAACGATCGGAGGACCGAAGGAGCTAACCGCTTTTTCACAAACATGGGGATCATGTAACTCGCCTTGATCGTTGGGAACCGGAGCTGAATGAAGCC 1100

PvuI

beta-lactamase

Fig. 21B

CCGTGGGGCTGGTGGCGCGGTGGCTGACGAGAGCGGCCACGTAGTGTGGCTGGCTCCCGCGGCTGAGACACCCATGACGCTCAGCTACATCCGCTACGA 3400

HC stuffer

GGTGGACGCTCTCGGCCGCAACGGCGCAGGGAGCGTACAGAGGGTGGAGATCTCGAGGGCGCACCGAGTGTGTCTGAGCAACCTGCGGGGCTCGGACG 3500

HC stuffer

CGCTACACCTTCGCGGTCGCGCGGTATGGCTGAGCCGAGCTTCGGCGGCTTCGGAGCGCTGGTGGAGCGCTGTGTGGTGTGCTGACGCTAGCGACC 3600

HC stuffer

TGACCCCTCATCTGACGCTCTCCCTCATCTCGTGGTATCCTGGTGTGCTGACCGTGTCTCGCGCTGCTCTCCACCGCGGGCTCTGAAGCAGAA 3700

HC stuffer

GATCTGGCTGGCATCCGAGCCAGAGAGCGAGTTGAAGGCTCTTCACCCACCCACAGGGTAACCTCCAGCTGTGGCTGTACCAATGATGGCTGC 3800

HC stuffer

CTGTGGTGGAGCCCTGCACCCCTTCACGGAGGACCCACCTGCTCCCTGGAGTCTCTCAGAGCGCTGCTGGGGGACGATGCAGGAGTGGAGCCGG 3900

HC stuffer

Fig. 21C

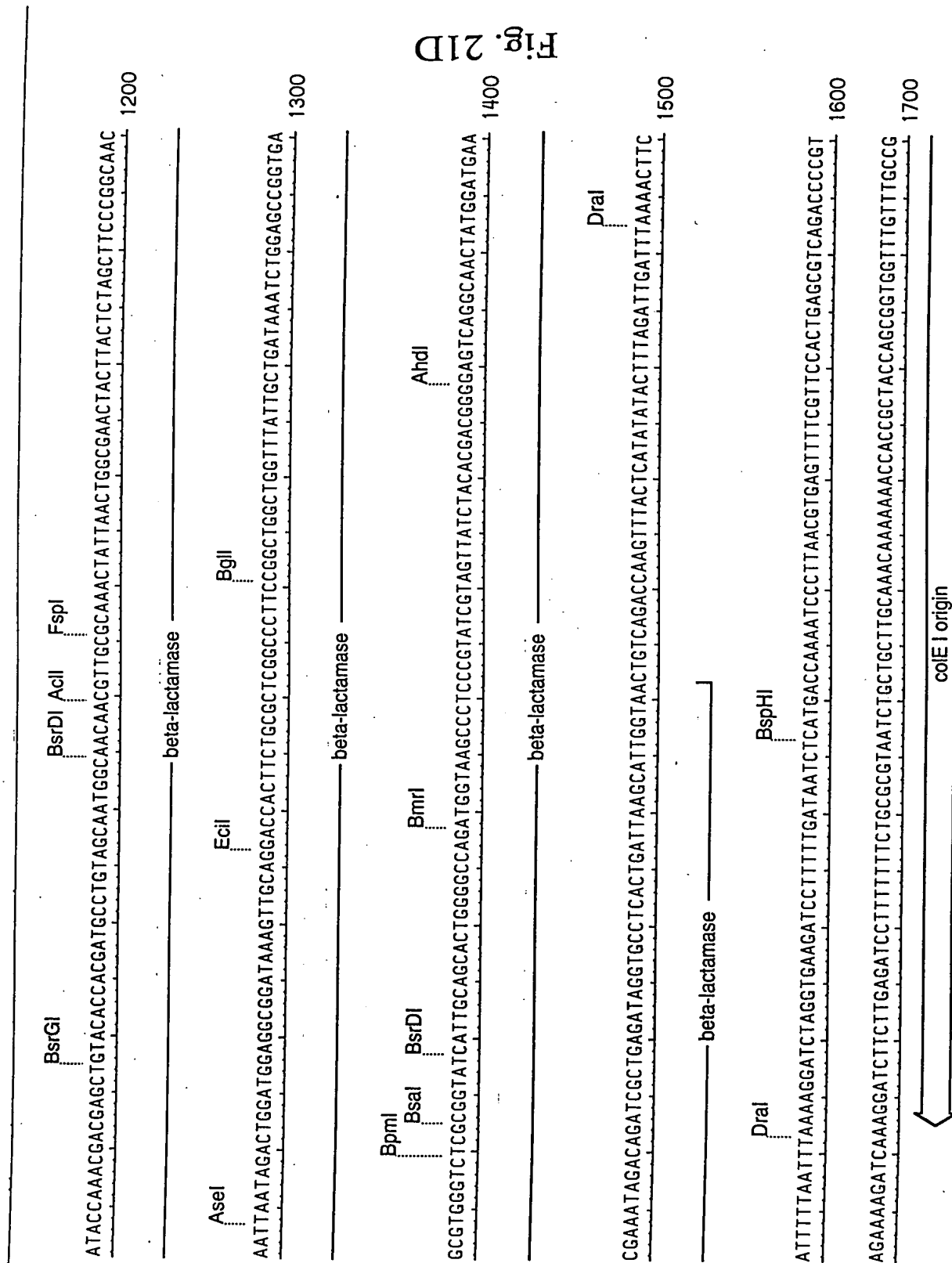


Fig. 21D

Ec0571

GATCAAGAGCTACCAACTCTTTTCCGAAGTAACTGGCTTCAGCAGAGCGCAGATACCAATACTGTCTTCTAGTGTAGCGGTAGTTAGGCCACCACCT

colE1 origin

AlwNI

TCAAGAACTCTGTAGCACC GGCTACATACCTGCTCTGCTAA TCTGTTACCA GTGGCTGCTGCCAGTGGCGATAAGTCGTGTCTTACCGGTTGGACTC

colE1 origin

Apali!

AAGACGATAGTTACCGGATAGGGCGCAGCGGTCGGGCTGAACGGGGGGTTCTGTCACACAGCCAGCTTGGAGCGAACGACCTACACCGAACTGAGATAC

colE1 origin

EciI BciVI

Res.

CTACAGCGTGACTATGAGAAAGCGCCACGCCTTCCGAAGGGAGCAAAGGCCGACAGGTATCCGGTAAGCGGCAGGGTCGGAAACAGGAGAGC GCACGAGGG

cole | origin

Drdi

AGCTTCCAGGGGAAACGCCCTGGTATCTTTATAGTCTGTCGGGTTCCGCCACCTCTGACTTGAGCGTCGATTTTGTGATGCTCGTCAGGGGGGGCGGAG

col/E1 origin

licil

Phil

CTATGGAAACGCCAGCAACGGGGCTTTTACGGTTCTTGGCCTTTTCCTGACATGTTCTTTCCTGGCTTATCCCGTATTCTGTG

COLE | origin

Fig. 21E

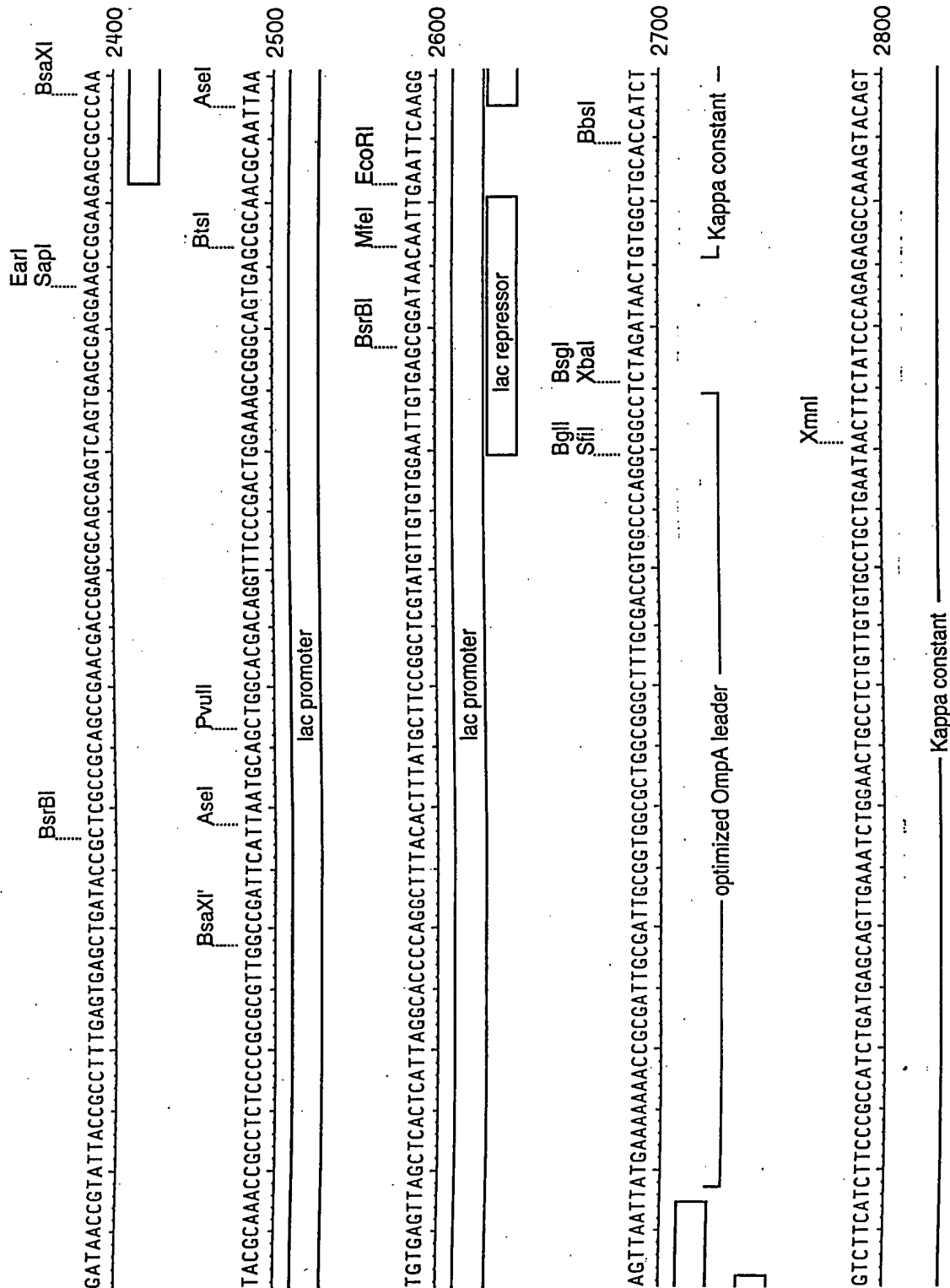


Fig. 21F

GGAAGGTGGATAACGCCCTCCAAATCGGGTAACTCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCCTACAGCCTCAGCAGCACCCCTGACGCT 2900

BbvCI Bpu10I BplI

Kappa constant

AlwNI Bpu10I EcoICRI SacI

GACCAAGCAGACTACGAGAAACACAAAGTCTACGGCTGCGAAGTCAACCCATCAGGGCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGTGT 3000

Kappa constant

EagI NotI

NgoMIV NaeI

SacI

TAAGCGCGCACTAGATATAATTAAGGAGATAAATATGAAATATCTGCTGCCGACCGCGGGCGGCCCTGCTGCTGCTGGCGGCGCAGCGCGCGATGG 3100

rfb

optimized pel B leader

XhoI NcoI BsgI

BssSI

BcgI BtrI

CGCTCGAGCTGATGAGCCATGGAAGCTGTGTGCGCTGCACACAGGCTCCACAGGCTCGTGGTGGGTGCGCTTCTGGTGTTCGCTGCGCTACAGCCGACACG 3200

HC stuffer

BcgI'

EcoRV

TCGAGCTTCGTGCCCCCTAGAGTTGCGCGTACACAGCAGCCTCCGGCGTCCGGGATATCACCGGTGTCATCCACATCAATGAAGTAGTGCTCCTAGACGCCCC 3300

HC stuffer

Fig. 21G

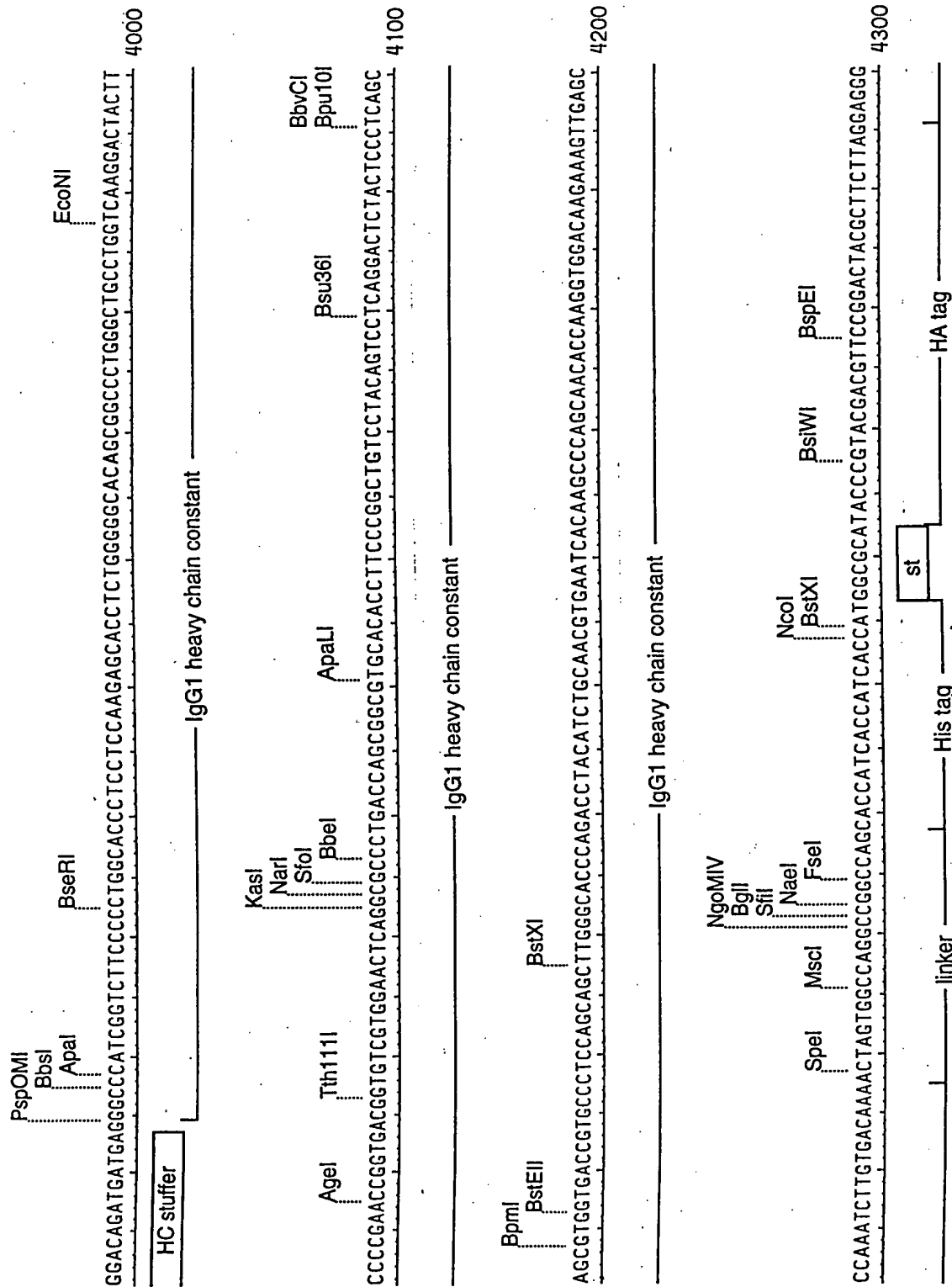


Fig. 21H

4400
TGGTGGCTCTGAGGGTGGCGGTTCTGAGGGTGGCGGCTCTGAGGGAGGCGGTTCCGGTGGCTCTGGTTCCGGTGATTTTGATTATGAAAAGATGGCA

gene III

4500
AACGCTAATAAGGGGGCTATGACCGAAAAATGCCGATGAAACGCGCTACAGCTGACGCTAAAGGCAAACTTGATTCTGTGCTACTGATTACGGTGCTG

gene III

4600
CTATCGATGGTTTCATTGGTGACGTTTCCGGCCTTGCTAATGGTAATGGTGTGCTACTGGTGATTTTGGTGGCTCTAATTTCCCAAATGGCTCAAGTCGGTGA

Clal

gene III

4700
CGGTGATAATTCACCTTTAATGAATAATTCGGTCAATATTTACCTTCCCTCCCTCAATCGGTTGAATGTGCGCCCTTTTGCTCTTACGCGCTGGTAAACCA

XmnI BsaXI SspI

BsaXI

AfeI

NdeI

gene III

4800
TATGAATTTTCTATTGATGTGACAAAAATAACTTATTCGGTGGTGCTTTTGGCTTTCTTTTATATGTTGCCACCTTTATGTAATTTTCTACGTTTG

gene III

4883
CTAACATACTGCGTAATAAGGAGTCTTAAGCTAGCTAATTAATTAAGCGCGCGCCGCGAGATCTGCTCTCTGAGGAGGATCT

EagI

NgoMIV

EagI

NaeI

FseI

BglII

Asel

AflIII NheI

Fig. 211